August 5, 2008

Ian Bartlett, Ph.D.
Lead Contact, Trimethyl Phosphite HPV Consortium
Product Stewardship Manager
Rhodia Inc.
8 Cedar Brook Drive
Cranbury, NJ 08512-7500

Dear Dr. Bartlett:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Trimethyl Phosphite, posted on the ChemRTK HPV Challenge Program Web site on February 7, 2006. I commend the Trimethyl Phosphite HPV Consortium for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that the Consortium advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. EPA has moved energetically from the HPV Challenge Program to the Chemical Assessment and Management Program, or ChAMP (www.epa.gov/champ) and is relying on Challenge chemical sponsors to provide, as expeditiously as possible, the data that are the key to this effort.
Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact me at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Mark W. Townsend, Chief
HPV Chemicals Branch

Enclosure

cc: R. Lee
J. Willis

EPA Comments on Chemical RTK HPV Challenge Submission:
Trimethyl Phosphite

Summary of EPA Comments

The sponsor, The Trimethyl Phosphite Consortium, submitted a test plan and robust summaries to EPA for trimethyl phosphite (TMP; CAS No. 121-45-9) dated December 21, 2005. Supporting data were also provided for the proposed analog, dimethyl phosphonate (DMHP; CAS No. 868-85-9). EPA posted the submission on the Chemical RTK HPV Challenge Web site on February 7, 2006.

EPA has reviewed the submission and has reached the following conclusions:

1. Analog Justification. The use of DMHP data to support TMP is reasonable.

2. Physicochemical Properties and Environmental Fate. Adequate data were submitted for all SIDS endpoints for the purposes of the HPV Challenge Program.

3. Health Effects. Adequate data were submitted for the acute, repeated-dose, gene mutations and developmental toxicity endpoints. EPA disagrees with the proposed *in vivo* testing for the chromosomal aberrations endpoint in favor of *in vitro* testing. The submitted data for TMP for the reproductive toxicity endpoint are inadequate; however, supplemented by available data for DMHP and methanol, this endpoint has been adequately addressed for the purposes of the HPV Challenge Program.

4. Ecological Effects. Adequate data were submitted for these endpoints for the purposes of the HPV Challenge Program.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on Trimethyl Phosphite Challenge Submission

Test Plan

Analog Justification

The proposed analog, DMHP, is the first-stage hydrolysis product of the sponsored substance, together with methanol (CAS No. 67-56-1). Both hydrolysis products have been assessed in the OECD HPV program and their data sets can be viewed at the following link: http://cs3-hq.oecd.org/scripts/hpv/. Trialkyl phosphites are well known to hydrolyze readily, with the initial reaction producing a dialkyl phosphonate, $(RO)_2P(H)=O$, that can then hydrolyze further. For TMP, the initial reaction to form DMHP occurs in minutes over a range of pH. EPA therefore agrees that the use of DMHP data is appropriate for the ecotoxicity endpoints and to support certain health effects endpoints.

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

Adequate data were submitted for the SIDS endpoints for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation and fugacity)

Adequate data were submitted for the SIDS endpoints for the purposes of the HPV Challenge Program.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity and reproductive/developmental toxicity)

Adequate data were submitted for the acute, repeated-dose, gene mutations and developmental toxicity endpoints.

Chromosomal aberrations. The submitter proposes *in vivo* testing of TMP for this endpoint using OECD TG 474. EPA disagrees with the proposed testing and recommends that the data for this endpoint be provided using the *in vitro* mammalian chromosome aberration test according to OECD TG 473.

Reproductive toxicity. The submitted data for the reproductive toxicity endpoint are inadequate for the purposes of the HPV Challenge program. Data from histopathological evaluations in 90-day repeated-dose toxicity studies are only adequate when no effects on the gonads are observed and in the absence of any developmental toxicity. For TMP, adverse effects were observed in the gonads and in the developmental toxicity study. Data for DHMP and methanol (http://cs3-hq.oecd.org/scripts/hpv/) indicate reproductive/developmental toxicity which supports the conclusion that TMP adversely affects reproduction. Therefore, no further testing is needed for the purposes of the HPV Challenge program.

Ecological Effects (fish, invertebrate and algae)

EPA agrees that the submitted acute toxicity data for the TMP hydrolysis product DMHP for fish, daphnia and algae are adequate for the purposes of the HPV Challenge Program.

Specific Comments on Robust Summaries

None

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.